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**A population of Nestin-expressing progenitors in the cerebellum exhibits increased tumorigenicity.**

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**Public Summary:**

It is generally believed that cerebellar granule neurons originate exclusively from granule neuron precursors (GNPs) in the external germinal layer (EGL). Here we identified a rare population of neuronal progenitors in mouse developing cerebellum that expresses Nestin. Although Nestin is widely considered a marker for multipotent stem cells, these Nestin-expressing progenitors (NEPs) are committed to the granule neuron lineage. Unlike conventional GNPs, which reside in the outer EGL and proliferate extensively, NEPs reside in the deep part of the EGL and are quiescent. Expression profiling revealed that NEPs are distinct from GNPs and, in particular, express markedly reduced levels of genes associated with DNA repair. Consistent with this, upon aberrant activation of Sonic hedgehog (Shh) signaling, NEPs exhibited more severe genomic instability and gave rise to tumors more efficiently than GNPs. These studies revealed a previously unidentified progenitor for cerebellar granule neurons and a cell of origin for medulloblastoma.

**Scientific Abstract:**

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